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Neutron and Proton Therapy in the Treatment of Cancer

Arlene Lennox

Fermi National Accelerator Laboratory
P.O. Box 500, Batavia, Illinois 60510

Saint Joseph Hospital
Elgin, Illinois 60123

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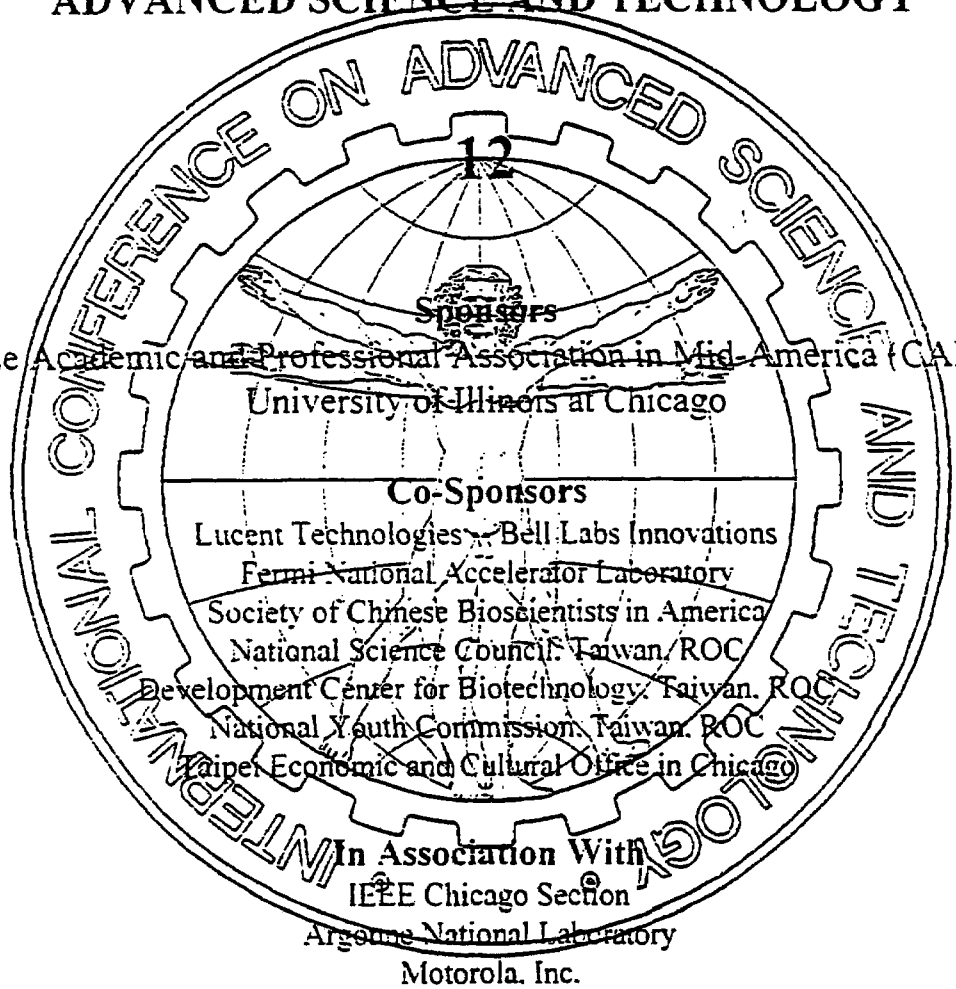

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NEUTRON AND PROTON THERAPY IN THE TREATMENT OF CANCER

Arlene J. Lennox
Fermi National Accelerator Laboratory, Batavia, Illinois and Saint Joseph Hospital, Elgin, Illinois

Abstract

Several decades of clinical research have established that neutron and proton therapy constitute useful and practical additions to the radiation oncologist's treatment modalities. This paper discusses the rationale for using these therapies and describes practical solutions to their implementation.

Rationale for Neutron and Proton Therapy

Use of x-rays (low energy photons) to treat cancerous tumors and other diseases began within months after their discovery by Roentgen in 1895. Since then a great deal of progress has been made in the design of accelerators to increase the energy (and hence the penetration ability) of the photons. Engineering improvements in patient positioning and the development of CT scanners for quality imaging have facilitated more precise dose delivery systems. A useful summary of these advances is given by Orton.[1] At present the limits to further improvement in radiation therapy with photons are associated with the physical and biological properties of the photons themselves, rather than their beam delivery systems. Neutron therapy addresses the biological limitations and proton therapy addresses the physical limitations. Clinical research has established that some tumors are radioresistant, that is, they are not controlled by conventional photon radiation. Many of these radioresistant tumors can be controlled by fast neutron therapy. Tumors that are close to critical structures such as the eye or central nervous system are often underdosed (and, therefore, not controlled) because a tumoricidal dose would cause unacceptable damage to the neighboring critical structure. Proton therapy takes advantage of the Bragg peak in its dose distribution to dramatically limit the dose to neighboring tissue so that an adequate dose can be delivered to the tumor. An extensive discussion comparing photon, neutron and proton radiation is given by Petti and Lennox.[2] It is important to understand the distinctions: (1) Photons and neutrons have the same dose distribution characteristics but neutrons are more biologically effective at killing tumors; (2) Photons and protons share the same biological effectiveness, but protons have superior dose distribution characteristics.

Present Implementation of Neutron and Proton Therapy

Within the past 10 to 15 years both neutron and proton therapy have become standard forms of therapy for certain tumors and ongoing clinical work is demonstrating their value for additional tumor types and sites. For example, clinicians are beginning to recognize the advantages of using neutron therapy combined with chemotherapy for palliation in cases where large tumors have already metastasized to distant sites. These therapies are no longer considered to be experimental and in the United States the treatments are reimbursed by Medicare and commercial insurance companies. A list of currently active proton and neutron treatment centers is given in Table 1. Each of these facilities uses a one-of-kind accelerator to deliver the beam and each has characteristics which should be well understood by any one contemplating the construction of a new facility. At present the only facility offering both proton and neutron therapy in a routine manner is the National Accelerator Centre in South Africa. Reference 2 describes the accelerators in more detail and lists additional sources of information.

Future Implementation of Neutron and Proton Therapy

If patients are to receive the best possible therapy for cancer it is imperative that they have access to a cancer treatment center that provides all the options, including surgery, chemotherapy, hyperthermia, brachytherapy and teletherapy. Unfortunately, in the present clinical environment, patients tend to receive the type of therapy which is available to the physician they first consult. It is sometimes difficult for the patient to obtain information on other options. Published results of clinical trials are available for a limited set of tumors. These are summarized in Table 2. However, there are cases where a physician may judge that particle therapy is appropriate even without published results of a clinical trial. For example, neutrons have an advantage over photons for local control of salivary gland tumors and advanced prostate cancer. Most of these tumors are adenocarcinomas, so one could conclude that neutrons may have a better chance of controlling adenocarcinomas appearing in other parts of the body. Protons have a demonstrated advantage over photons in uveal melanoma and clival chordoma. In both cases the dose distribution advantage enables the physician to prescribe a higher tumor dose than would be reasonable with photons. One could conclude that any tumor close to a critical structure could be given a higher dose with protons and thus protons would have a better chance for tumor control. Because there are many variables in the way the dose is delivered it can be hard to determine whether an advantage is due to the particles or to the dose delivery techniques. This issue can best be resolved if the same investigators are involved in both the photon and particle arms of the protocol. A comprehensive cancer center which treats all forms of cancer, can provide optimal care if it has access to photon, neutron and proton teletherapy.

Table 1. Proton and neutron treatment centers.

Particle	Location	Accelerator Type	Beam Energy (MeV)
neutrons	Cape Town, South Africa	Separated Sector Cyclotron	66 MeV p + Be
neutrons	Batavia, Illinois	Proton Linac	66 MeV p + Be
neutrons	Detroit, Michigan	Superconducting Cyclotron	48 MeV d + Be
neutrons	Seattle, Washington	Cyclotron	50 MeV p + Be
neutrons	Beijing, China	Proton Linac	30 MeV p + Be
protons	Cambridge, MA	Synchrocyclotron	160
protons	Sweden	Cyclotron	200
protons	Moscow, Russia	Synchrotron	70-200
protons	St. Petersburg, Russia	Synchrocyclotron	1000
protons	Chiba, Japan	Cyclotron	70
protons	Tsukuba, Japan	Synchrocyclotron	250
protons	Villigen, Switzerland	Cyclotron	72
protons	Merseyside, England	Cyclotron	62.5
protons	Davis, California	Cyclotron	67.5
protons	Loma Linda, CA	Synchrotron	70 - 250
protons	Nice, France	Cyclotron	63
protons	Orsay, France	Cyclotron	200
protons	Cape Town, South Africa	Separated Sector Cyclotron	200
protons	Louvain-la-Neuve, Belgium	Cyclotron	90

Because particle therapy is a relatively new form of teletherapy there is still a great deal of discussion as to the optimal accelerator for generating the therapy beams. With regard to proton therapy there are proponents of both cyclotrons and synchrotrons. If scattering techniques are used to spread out the Bragg peak cyclotrons have an advantage because high intensities are easier to achieve, making it easier to compensate for the beam which is lost in the scatterer. On the other hand scanning techniques which make more efficient use of the beam work best with pulse-to-pulse energy variation, which is not readily accomplished with a cyclotron. Fast neutron therapy is accomplished using cyclotrons or linacs. A cost-effective way to provide both proton and neutron therapy at a single facility is to use a ~70 MeV proton linac as injector to a synchrotron. The experience at Fermilab, where the linac provides beam for the Neutron Therapy Facility and serves as an injector for a high energy synchrotron, demonstrates that it is possible to switch the beam between the two applications at a 15 Hz rate without human intervention. Thus, a neutron patient and a proton patient can receive therapy at the same time, completely eliminating scheduling conflicts. Access to a 70 MeV beam also allows for the production of longer lived isotopes for imaging or basic research. These isotopes cannot be produced by the standard 10-15 MeV cyclotrons used for positron emission tomography (PET). Since they are long-lived they could be sold to researchers, providing a source of revenue without interfering with patient treatments. More details on a combined proton/neutron therapy facility are given in reference 3.

Table 2. Some tumors appropriate for particle therapy as demonstrated by published clinical trials.

Neutrons	Protons
Salivary gland tumors including adenocarcinoma, adenoid cystic carcinoma, pleomorphic adenoma	Uveal melanoma
Head and neck cancer including non-resectable or recurrent non-epidermoid, squamous cell	Skull-base tumors including chordoma, chondrosarcoma, meningioma, craniopharyngioma, pituitary adenoma
Advanced prostate cancer	Arteriovenous malformations
Sarcoma of soft tissue and bone	Esophageal cancer
Non-small cell lung cancers	
Pancreatic Cancer	
Malignant melanoma	

Summary and Discussion

Over twenty years of research with proton and neutron therapy have shown that both modalities offer superior radiation treatment for several types of tumors. The capital investment for a particle therapy facility is high compared to photon therapy but once the initial investment is made operating costs can be recouped from patient payments. Heavy ion therapy with particles such as neon or carbon combines the dose distribution advantages of protons with the biological effectiveness of neutrons. However, at this time the cost of a heavy ion facility is so much greater than proton or neutron therapy that it is out of reach for most medical centers. In addition, much remains to be done establishing treatment techniques and protocols to find a niche for heavy particle therapy. Fortunately, the Chiba and Darmstadt facilities are in a position to continue the heavy ion research while other centers are starting to make proton and neutron therapy more available to the public. Individuals planning a new center can take advantage of the experience at existing facilities but because each of these facilities is unique one must be careful to understand the advantages and disadvantages of each before finalizing construction plans.

References

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